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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,819	05/19/2000	Frank P. Luyten	NIH0099.001C1	1648

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EXAMINER

ROMEO, DAVID S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/574,819

Applicant(s)

LUYTEN ET AL.

Examiner

David S Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

The amendment filed 10/02/2003 has been entered. Claims 27-32 are pending and being examined.

5 **Maintained Formal Matters, Objections, and/or Rejections:**

Claim Rejections - 35 USC § 102

Claim 27 is rejected under 35 U.S.C. 102(a) as being anticipated by Storm (38, cited by Applicants).

Applicant argues that the rule 131 declaration shows as much of the claimed
10 invention as is described in Storm at a date prior to 01/12/1993, and, therefore, the rejection is overcome. Applicant's arguments have been fully considered but they are not persuasive for the reasons discussed below regarding the insufficiency of the declaration.

Claim Rejections - 35 USC § 103

15 Claims 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storm (38, cited by Applicants) and Neidhardt (9, cited by Applicants). Applicant argues that the rule 131 declaration shows as much of the claimed invention as is described in Storm at a date prior to 01/12/1993, and that the secondary reference does not fill in the gap left by antedating the primary reference. Applicant's arguments have been fully
20 considered but they are not persuasive for the reasons discussed below regarding the insufficiency of the declaration.

Response to Amendment

The declaration filed on 10/02/2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Storm reference.

The declaration is insufficient because the scope of the declaration or affidavit is
5 not commensurate with the scope of the claims.

The present claims are directed to an isolated DNA molecule which codes for a protein of the TGF- β family, wherein said protein has chondrogenic activity in vivo and comprises the amino acid sequence of SEQ ID NO: 24.

The present specification discloses that bone morphogenetic proteins (BMPs) are
10 members of the TGF- β superfamily that can induce endochondral bone formation in adult animals. This superfamily includes a large group of structurally related signaling proteins that are secreted as dimers and then cleaved to result in biologically active carboxy terminal domains of the proteins. These bioactive proteins are characterized by
7 highly conserved cysteine residues. See page 1, lines 7-11.

15 Two novel members of the TGF- β superfamily were identified and designated Cartilage-Derived Morphogenetic Protein-1 (CDMP- 1), and -2 (CDMP-2). The C-terminal TGF- β domains of these proteins were 82% identical, thus defining a novel subfamily most closely related to BMP-5, BMP-6 and osteogenic protein-1. See page 5, lines 4-7.

20 The nucleotide sequence and the translation of the open reading frame of CDMP-1 are presented in Figure 1. The CDMP-1 protein was predicted to have 500 amino acids, to consist of a pro-region of 376 amino acids, a typical cleavage site (Arg-Xaa-Xaa-Arg/Ala) (SEQ ID NO:9), and a C-terminal domain of 120 amino acids containing the

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seven highly conserved cysteines characteristic of the TGF- β gene family. See page 10, lines 11-16.

Alignment of the carboxy terminal domains of CDMP-1 and -2 with other members of the BMP family revealed an amino acid identity of about 50% with BMP-5, BMP-6 and OP-1 (BMP-7). These results suggested that CDMP-I and CDMP-2 are members of a new subfamily. See page 10, last full paragraph.

In general, BMPs are dimeric molecules. The dimeric conformation is critical for biological action. BMP monomers are processed to yield the C-terminal mature monomer of 110+ amino acids. See Reddi (31, cited by Applicants) page 13, left column, last full paragraph.

Thus, one would expect that an isolated DNA molecule which codes for a protein of the TGF- β family, wherein said protein has chondrogenic activity in vivo, as claimed, would code for a protein that is secreted as a dimer and then cleaved to result in a biologically active carboxy terminal domain of 110+ amino acids, characterized by 7 highly conserved cysteine residues.

The declaration only sets forth nucleic acid molecules encoding amino acid sequences that are approximately 40 amino acids in length. One would not expect that these approximately 40 amino acid peptides would have chondrogenic activity in vivo because one would expect that an isolated DNA molecule which codes for a protein of the TGF- β family, wherein said protein has chondrogenic activity in vivo, would code for a protein that is secreted as a dimer and then cleaved to result in a biologically active carboxy terminal domain of 110+ amino acids, characterized by 7 highly conserved cysteine residues. No evidence has been brought forth that these approximately 40 amino

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acid peptides would provide a protein that has chondrogenic activity in vivo. Thus, the scope of the declaration or affidavit is not commensurate with the scope of the claims.

In addition, the declaration actually shows less than the Storm reference, because the declaration only shows nucleic acid molecules encoding amino acid sequences that are approximately 40 amino acids in length, which would not be expected to have chondrogenic activity in vivo, whereas Storm shows an isolated DNA molecule which codes for a protein of the TGF- β family that is secreted as a dimer and then cleaved to result in a biologically active carboxy terminal domain of 110+ amino acids, characterized by 7 highly conserved cysteine residues, which would be expected to be active in vivo. A chemical composition and its properties are inseparable. Therefore, the properties applicant discloses and/or claims, i.e. "has chondrogenic activity in vivo", are necessarily present in Storm's GDF-6.

In conclusion, the declaration is insufficient to antedate the Storm reference.

15

Conclusion

No claims are allowable.

20

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than

5 SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

10 IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306

15 AFTER FINAL (703) 872-9307

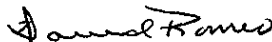
IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

20 FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

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DAVID ROMEO
PRIMARY EXAMINER
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DSR
JANUARY 4, 2004